TABLE I. Hematological and Biochemical Values and γ-Globin Chain Percentages

Patient	I_1	II_1	II_2
Sex/age (years)	F/40	M/18	M/16
Hb g/dl	9.7	11.1	10.1
PCV l/l	0.305	0.32	0.36
RBC 10^{12}/l	4.59	5.26	5.2
MCV fl	64	61	70
MCH pg	17	19.8	20
Hb A_2 %	5.6	5.8	5.3
Hb F %	0.9	1.1	1.6
$^{A}\gamma^{T}$ %	57.5	44.5	41.2
$^{A}\gamma^{I}$ %	16.5	17.4	17.7
$^{G}\gamma$ %	26	38.1	41.1

Alleles" [1]. The authors report the frameshift CD 11 (−T) β-thalassemia mutation in a father and 2 children of Mexican mestizo lineage and in one of them, this mutation is associated with the −28 A→C β-thalassemia mutation, producing a picture of β-thalassemia major. Moreover, the authors indicate that the frameshift CD 11 (−T) mutation has not been reported in any other population. In this sense, in a study of 141 β-thalassemia alleles we found the frameshift CD 11 (−T) allele in a family (mother, I_1, and 2 children, II_1 and II_2) from Caceres (Extremadura, western Spain) [2]. In this family the frameshift CD 11 (−T) allele was linked to the same haplotype (−++−−++−), analyzing the following polymorphic sites: *Hinc*II 5′ to the ϵ gene, *Hind*III in the IVS of $^{G}\gamma$ and $^{A}\gamma$ genes, *Hinc*II in the ψβ gene and 3′ to it, *Ava*II site in the IVS-2 of the β gene, and *Hpa*I and *Bam*HI 3′ to the β gene.

The 3 patients were diagnosed with heterozygous β^0-thalassemia with high HbA_2, a clinical picture more severe than β-thalassemia minor. The study by Southern blot of α genes proved the existence of four genes α.

The hematological and biochemical values and the γ-globin chain percentage are shown in Table I. The molecular identification of the β-thalassemia allele was performed by direct sequencing of amplified β-gene DNA, because the lesion had not been detected by PCR-ARMS studying 24 known β-thalassemia alleles.

The family comes from Caceres (Extremadura, western Spain). Many of the men who went to America in the fifteenth and sixteenth centuries came from this region [2]. Due to this fact, it would be interesting to pursue more studies in order to know if the real origin of this mutation is proper to the Mexican etnia or has its origin in Spain, where it has been proved that β-thalassemia is relatively frequent [3].

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Reply to "Frameshift Cd 11 (−T) β-Thalassemia Mutation"

To the Editor: In regard to the letter by Villegas et al. about our article in the *American Journal of Hematology* [1], I regret not including the paper by Ropero et al. [2]. However, this letter gives us the opportunity to make some comments. In the original paper [2], the Cd 11 (−T) mutation was found in 1 of 60 studied β-thalassemia patients (67 chromosomes analyzed), in whom eight different alleles were found, with three alleles constituting almost 90% of the analyzed chromosomes (IVS1:1 G→A, Cd 39 C→T, and IVS1:6 T→C). In their letter, Villegas et al. report additional studies on 74 chromosomes without finding the mutation in them, thus indicating that Cd 11 (−T) is a rare mutation in this area. The data about β-haplotypes referred to in that letter are very interesting, because Cd 11(−T) is the same haplotype found in our patient; however, since this haplotype was also found with β^A chromosomes in our Mestizo population, the possibility that the mutation appeared in both countries at different times cannot be ruled out. This could be posteriorly investigated by the recently discovered polymorphisms surrounding the β-globin gene [3]. Moreover, it is very interesting that the 3 Cd 11 (−T) carriers from Spain and at least 1 of the 2 carriers in our family [1] had a clinical picture more severe than the common β-thalassemia heterozygotes, which apparently cannot be explained by the mutation per se. The possibility that in both families the Cd 11 (−T) mutation is associated with an additional pathology, making the clinical picture more severe, is also a matter of further investigation, and these data could also give us more information about the origin of the mutation.

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